Mesenchymal stem cells for the sustained in vivo delivery of bioactive factors.

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Public Summary:
Mesenchymal stem cells (MSC) are a promising tool for cell therapy, either through direct contribution to the repair of bone, tendon and cartilage or as an adjunct therapy to secrete factors to heal tissues. Following transplantation, MSC are capable of systemic migration, are not prone to tumor formation, and appear to tolerize the immune response to allow transplantation from non-matched donors. MSC preferentially migrate to areas of tissue damage and low oxygen. We describe work done by our group and others in using human MSC for the sustained in vivo production of supraphysiological levels of cytokines for the support of cotransplanted hematopoietic stem cells and enzymes that are deficient in animal models of lysosomal storage disorders such as MPSVII. In addition, the use of MSC engineered to secrete protein products is reviewed in several fields of tissue injury repair, including but not limited to revascularization after myocardial infarction, regeneration of intervertebral disc defects and spine therapy, repair of stroke, therapy for epilepsy, skeletal tissue repair, chondrogenesis/knee and joint repair, and neurodegenerative diseases. Genetically engineered MSC have proven safe and effective in numerous animal models of disease modification and tissue repair and are poised to be tested in human clinical trials. The potential for these interesting cells to secrete endogenous or transgene products in a sustained and long-term manner is highly promising.

Scientific Abstract:
Mesenchymal stem cells (MSC) are a promising tool for cell therapy, either through direct contribution to the repair of bone, tendon and cartilage or as an adjunct therapy through protein production and immune mediation. They are an attractive vehicle for cellular therapies due to a variety of cell intrinsic and environmentally responsive properties. Following transplantation, MSC are capable of systemic migration, are not prone to tumor formation, and appear to tolerize the immune response across donor mismatch. These attributes combine to allow MSC to reside in many different tissue types without disrupting the local microenvironment and, in some cases, responding to the local environment with appropriate protein secretion. We describe work done by our group and others in using human MSC for the sustained in vivo production of supraphysiological levels of cytokines for the support of cotransplanted hematopoietic stem cells and enzymes that are deficient in animal models of lysosomal storage disorders such as MPSVII. In addition, the use of MSC engineered to secrete protein products has been reviewed in several fields of tissue injury repair, including but not limited to revascularization after myocardial infarction, regeneration of intervertebral disc defects and spine therapy, repair of stroke, therapy for epilepsy, skeletal tissue repair, chondrogenesis/knee and joint repair, and neurodegenerative diseases. Genetically engineered MSC have thus proven safe and efficacious in numerous animal models of disease modification and tissue repair and are poised to be tested in human clinical trials. The potential for these interesting cells to secrete endogenous or transgene products in a sustained and long-term manner is highly promising and is discussed in the current review.